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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/234,532 | 01/21/1999 | ALFRED SAPSE | 1398-002 | 5965 |

7590 03/06/2003

JOSEPH A. MAHONEY
MAYER, BROWN, ROWE & MAW
P.O. BOX 2828
CHICAGO, IL 60690-2828

| EXAMINER |
|---|
| OWENS JR, HOWARD V |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1623 | 30 |

DATE MAILED: 03/06/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. 09/234,532 | Applicant(s) SAPSE, ALFRED | |
|---|---|---|---|
| | Examiner Howard V Owens | Art Unit 1623 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *16 September 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-3,5,10,11,13-15 and 21-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5,10,11,13-15 and 21-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Detailed Action

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/16/02 has been entered.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

**35 USC § 103**

Claims 1-3, 5, 10, 11, 13, 14 and 21-36 are rejected under 35 U.S.C. § 103 as being unpatentable over Devita et al., AIDS,4th edition, pp. 501-504, in combination with Beale, U.S. Patent No. 5,756,469 and Lemay et al., Int. Conf. AIDS, vol.5,1989.

Claims 1-3 are drawn to a composition comprising at least two anti-HIV drugs and a cortisol blocker.

Claims 5, 10, 11, 13 and 14 are drawn to a method for the management of side effects associated with the administration of anti-HIV drug therapy comprising administration to a patient a therapeutically effective amount of at least one cortisol blocker.

Claims 21-36 are drawn to various concentrations of the anti-HIV drug/cortisol composition.

Beale teaches the use of anti-cortisol compounds such as HMB, DHEA, Ipriflavone and phosphatidylserine in the treatment of patients with AIDS to reduce the catabolic effects associated with AIDS (col.2-col.8, line 19). Beale does not explicitly teach the use of anti-cortisol compounds in a composition with anti-HIV drugs.

Lemay et al. teach the cortisol blocker ketaconazole in combination with the anti- HIV drug Zidovudine (AZT).

Devita et al. teach that combinations of anti-HIV drugs are beneficial in treating HIV infection for several reasons: Two or more drugs may have additive or synergistic interactions that produce better efficacy than with either drug alone, lower doses than those employed in monotherapies- possibly decreasing toxicity, delaying the emergence of a resistant virus that can escape drug inhibition, and targeting of different cellular and tissue reservoirs of the virus; particularly AZT in combination with ddC, ddI or 3TC as the combination of AZT with these agents present stronger synergy over monotherapies or treatment of AZT resistant isolates (DeVita et al., AIDS, 4th edition, pp. 502-504).

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

A *prima facie* case of obviousness is supported when the prior art alone would have appeared to suggest doing, at the time the invention was made, what the applicant has done. It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made that a cortisol blocker could be used in a composition with an anti-HIV drug. One of skill in the art would have been provided with a clear motivation and a reasonable expectation of success to combine the teachings of Beale with that of Lemay and Devita given that any method of treatment would seek to reduce the catabolic effects associated therein, as Lemay and Devita teach the benefits of combination therapies wherein cortisol blockers are used in the treatment of HIV to increase the synergistic effects of an anti-HIV drug and cortisol blockers are shown by Beale to reduce the catabolic effects of the disease itself, whether the catabolic effects are associated with the use of the anti-HIV drug or the disease itself, one of skill would

include cortisol blockers in the treatment regime to reduce or alleviate these catabolic effects as an adjunct to a combination therapy.

The prior art need not explicitly state each side effect, only provide a motivation to combine the two compounds, in this case, applicant's side effects would be viewed as catabolic effects, and given that Lemay and Devita teach the benefits of combination therapies wherein cortisol blockers are used in the treatment of HIV to increase the synergistic effects of an anti-HIV drug and cortisol blockers are shown by Beale to reduce the catabolic effects of the disease itself, whether the catabolic effects are associated with the use of the anti-HIV drug or the disease itself, one of skill would include cortisol blockers in the treatment regime to reduce or alleviate these catabolic effects as an adjunct to a combination therapy.

**Declaration**

The rejection of claims 1-3,5,10,11,13 and 14 under 35 U.S.C. 103 is maintained for the reasons of record set forth in the advisory action mailed 11/13/00.

The declaration submitted states that the study supporting the beneficial results was released in May of 2000; however, other than the methodology of the experiment, the actual study or data was not provided to the examiner as factual evidence. To be of probative value, any objective evidence should be supported by actual proof; moreover, the declaration does not outweigh the evidence supporting the prima facie case of obviousness as set forth in the office actions mailed 3/2/00 and 7/21/00. The 35 U.S.C. 103 of record is not solely based upon administration of the compounds singularly, although applicant admits in p.2 of the instant reply that the specification teaches that the compounds may be administered separately or as "..a composition defined as having both components systemically in the human body".

As cited previously, Beale teaches the use of anti-cortisol compounds such as HMB, DHEA, Ipriflavone and phosphatidylserine in the treatment of patients with AIDS to reduce the catabolic effects associated with AIDS (col.2-col.8, line 19). Beale does not explicitly teach the use of anti-cortisol compounds in a composition with anti-HIV drugs.

Lemay et al. teach the cortisol blocker ketaconazole in combination with the anti-HIV drug Zidovudine (AZT).

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The test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

The prior art need not explicitly state each side effect, only provide a motivation to combine the two compounds, in this case, applicant's side effects would be viewed as catabolic effects, and given that Lemay and Devita teach the benefits of combination therapies wherein cortisol blockers are used in the treatment of HIV to increase the synergistic effects of an anti-HIV drug and cortisol blockers are shown by Beale to reduce the catabolic effects of the disease itself, whether the catabolic effects are associated with the use of the anti-HIV drug or the disease itself, one of skill would include cortisol blockers in the treatment regime to reduce or alleviate these catabolic effects as an adjunct to a combination therapy.

A *prima facie* case of obviousness is supported when the prior art alone would have appeared to suggest doing, at the time the invention was made, what the applicant has done. It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made that a cortisol blocker could be used in a composition with an anti-HIV drug. One of skill in the art would have been provided with a clear motivation and a reasonable expectation of success to combine the teachings of Beale with that of Lemay and Devita given that any method of treatment would seek to

reduce the catabolic effects associated therein, as Lemay and Devita teach the benefits of combination therapies wherein cortisol blockers are used in the treatment of HIV to increase the synergistic effects of an anti-HIV drug and cortisol blockers are shown by Beale to reduce the catabolic effects of the disease itself, whether the catabolic effects are associated with the use of the anti-HIV drug or the disease itself, one of skill would include cortisol blockers in the treatment regime to reduce or alleviate these catabolic effects as an adjunct to a combination therapy.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Howard V. Owens
Patent Examiner
Art Unit 1623

James O. Wilson
Supervisory Patent Examiner
Technology Center 1600

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Howard Owens whose telephone number is (703) 306-4538 . The examiner can normally be reached on Mon.-Fri. from 8:30 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the Supervisory Patent Examiner signing this action, James O. Wilson can be reached on (703) 308-4624 . The fax phone number for this Group is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.